

AMENDMENTS TO THE SPECIFICATION

At page 13, please replace the second full paragraph with the following amended paragraph:

Fig. 7 illustrates the cytotoxicity of a subline of an HLA-A2-restricted cytotoxic T lymphocyte OK-CTLd and T lymphocyte antigen receptor V β usages (TCR V β usages.) Fig. 7a illustrates the cytotoxicity of a pooled OK-CTLd subline against T2 cells pulsed with each of five peptides or with a peptide derived from human immunodeficiency virus (HIV) (SLYNTYATL designated SEQ ID NO:409) used as a negative control (n.c.). In this figure, the Y-axis denotes percentage of ^{51}Cr released from T2 cells, i.e., specific cytolytic activity; and the X-axis denotes the ratio of effector cells to target cells (E/T ratio.) Fig. 7b illustrates TCR V β usages of peripheral blood mononuclear cells (OK-PBMC) derived from a cancer patient OK, OK-CTLd-6, OK-CTLd-9, or sublines that were established from OK-CTLd, which were pooled as shown in the figure. In the figure, "non-reactive sublines" denote sublines that do not respond to the peptides, and numbers shown in the upper side denotes types of TCR V β .

At page 13, please replace the third paragraph that finishes at page 14 with the following amended paragraph:

Fig. 8 illustrates that peripheral blood mononuclear cells (PBMC), derived from a cancer patient, recognized each cDNA clone or each peptide in an HLA-A2-restricted manner. Fig. 8a illustrates that PBMC (OK-PBMC) derived from a cancer patient recognized COS-7 cells, into which a plasmid carrying each cDNA clone was co-transfected with HLA-A0207, resulting in enhancement of IFN- γ production from the PBMC. Fig. 8b illustrates that PBMC derived from a

cancer patient recognized COS-7 cells, into which HLA-A0207 was transfected and pulsed with a peptide, resulting in enhancement of IFN- γ production from the PBMC. SLYNTYATL (SEQ ID NO: 409) was used as a negative control.

At page 14, please replace the third full paragraph with the following amended paragraph:

Fig. 11 illustrates that peptides derived from cDNA clone SW620-cl.48 (SEQ ID NOS: 409-413, 364-365, 414, 366-367, 415-420 and 368-369, from top to bottom), which is derived from a human colon cancer, were recognized by HLA-A2-restricted cytotoxic T lymphocyte OK-CTLd, and enhanced IFN- γ production from OK-CTLd.

At page 14, please replace the fifth full paragraph with the following amended paragraph:

Fig. 13 illustrates that peptides derived from a cDNA clone KE4-cl.21, which is derived from a human esophageal cancer, were recognized by an HLA-A26-restricted cytotoxic T lymphocyte KE4-CTL, and enhanced IFN- γ production from KE4-CTL. Fig. 13a and Fig. 13b show the results of two experiments. In Fig. 13a, '—●—' denotes KE4-21•P28, '—▲—' denotes KE4-21•P29, '—■—' denotes KE4-21•P39, and '—○—' denotes KE4-21•P40. The sequences are, from top to bottom, SEQ ID NOS: 403-404, 421-428, 405-406, 429-435 and 408. In Fig. 13b, '—●—' denotes KE4-21•P28, '—▲—' denotes KE4-21•P38, '—○—' denotes KE4-21•P40, and '—■—' denotes KE4-21•P47. The sequences are, from top to bottom, SEQ ID NOS: 403-404, 421-428, 406, 429-435, 408 and 405.

Please replace the first full paragraph on page 18 of the specification with the following amended paragraph:

Amino acid sequences (SEQ ID NO:214, SEQ ID NO:228, SEQ ID NO:269, SEQ ID NO:261, and SEQ ID NO:236) encoded by five genes (clone 12, clone 65, clone 81, clone 86, and clone 100) among the genes obtained by the present invention are identical to those encoded by known genes ID456, ID629, ID1226, ID163, and ID116, respectively, that were identified by the SEREX method and disclosed in the SEREX database (~~http://www-~~ludwig.unil.ch/SEREX.html). Moreover, nucleotide sequences (SEQ ID NO:289, SEQ ID NO:299, and SEQ ID NO:332) of clone 12, clone 82, and clone 86, are identical to those of ID456, ID1197, and ID163, respectively. In addition, it was revealed that clone 32, clone 41, clone 74, and clone 87 are partially homologous to ID1072, ID1233, ID979, and ID567, respectively.

Please replace the first full paragraph on page 29 of the specification with the following amended paragraph:

Identification of Tumor Antigen Peptide CTL

In order to obtain a tumor antigen peptide from amino acid sequences encoded by the above genes, an HLA-A2 binding motif (a specific sequence) was searched using the homepage (~~http://~~bimas.dcrf.nih.gov/molb-io/hla_bind/) of Bioinformatics & Molecular Analysis Section (BIMAS), and an amino acid sequence suitable for the motif was specified based on the amino acid sequences encoded by the above genes and the amino acid sequences of gene products of

genes highly homologous to the above genes. Based on the result, various peptides of 9-mer and 10-mer having an HLA-A2-binding motif were designed and synthesized.

Please replace the paragraph bridging pages 56 and 57 of the specification with the following amended paragraph:

With respect to each of the genes obtained, a homology search was carried out using GenBank/DDBJ, and the results obtained are summarized in Tables 1 to 6 above. Moreover, a homology search using the SEREX database (<http://www-ludwig.unil.ch/SEREX.html>) revealed that amino acid sequences encoded by clone 12, clone 65, clone 81, clone 86, and clone 100 1422 are identical to ones encoded by known genes ID456, ID629, ID1226, ID163, and ID116, respectively, which are disclosed in SEREX database. Moreover, the nucleotide sequences of clone 12, clone 82, and clone 86 are identical to those of ID456, ID1197, and ID163, respectively. In addition, it was found that clone 32, clone 41, clone 74, and clone 87 are partially homologous to ID1072, ID1233, ID979, and ID567, respectively.

Please replace the paragraph bridging pages 57 and 58 of the specification with the following amended paragraph:

Identification of HLA-A2-restricted Tumor Antigen Peptide

In order to obtain tumor-antigen peptides from tumor antigens encoded by genes obtained in Example 2, an HLA-A2 binding motif (a specific sequence) was searched for amino acid sequences encoded by the genes using a home page (http://bimas.dcrf.nih.gov/molbio/hla_bind/) of Bioinformatics & Molecular Analysis Section (BIMAS). The type of HLA of OK-CTLd is HLA-A0207, so that motif search was carried out for peptides capable of binding to HLA-A0207

molecule. HLA-A0207 molecule is different from HLA-A0201 molecule only in the 123rd amino acid residue in the amino acid sequence, which is Y in the sequence of the former and is C in the sequence of the latter. This amino acid residue is not located in an α -helix or β -sheet that is related with peptide binding, but is located in a coil region of the secondary structure, so that the difference of this amino acid residue does not affect the peptide binding. Therefore, a peptide that is suitable for an HLA-A0201-binding motif [Rammensee, H.-G. et al., Immunogenetics, 41: 178-228, 1995] would bind to HLA-A0207. Then, peptides capable of binding to an HLA-A0207 molecule were designed based on a result obtained by searching an HLA-A0201-binding motif, and various peptides of 9-mer and 10-mer (whose purity is 70% or higher) were synthesized by a well-known method. Moreover, with respect to clone 5, clone 23, clone 26, clone 35, clone 65, clone 81, and clone 100, peptides were designed and synthesized based on the amino acid sequences encoded by genes highly homologous to each gene.

At page 61, please replace the first full paragraph with the following amended paragraph:

Results with peptides derived from clone 2, clone 29, and clone 40 are representatively illustrated in Figs. 4, 5, and 6, respectively. In the figures, peptides recognized by OK-CTLd and judged as ones capable of activating OK-CTLd are shown with bold (solid) lines. A peptide (SLYNTVATL) (SEQ ID NO: 436) (negative control) derived from HIV (human immunodeficiency virus) that is suitable for an HLA-A2-binding motif was not recognized by OK-CTLd.

At page 69, please replace the third full paragraph that finishes on page 70 with the following amended paragraph:

Among the synthesized peptides (1.22 ng/ml to 20 µg/ml), peptides recognized by OK-CTLd in an HLA-A2-restricted manner were selected in a manner similar to Example 3. As a result, eighteen peptides of SEQ ID NO:364 to 381 in the sequence listing were recognized by OK-CTLd in a dose dependent manner and enhanced IFN-γ production from OK-CTLd, while a peptide (SLYNTVATL) (SEQ ID NO: 436) derived from HIV that was used in place of the above peptide as a negative control did not enhance IFN-γ production from CTL. The obtained eighteen peptides are SW620-48•P162, SW620-48•P163, SW620-48•P165, SW620-48•P166, SW620-48•P173, and SW620-48•P174 (SEQ ID NO:364 to 369) derived from SW620-cl.48 as well as SW620-121•P665, SW620-121•P666, SW620-121•P667, SW620-121•P668, SW620-121•P669, SW620-121•P676, SW620-121•P677, SW620-121•P678, SW620-121•P679, SW620-121•P685, SW620-121•P686, and SW620-121•P688 (SEQ ID NO:370 to 381) derived from SW620-cl.121. As representative data, Fig. 11 illustrates that six peptides derived from SW620-cl.48 were recognized by OK-CTLd in a dose dependent manner and enhanced IFN-γ production from OK-CTLd.